Comparison of 2 Correction Methods for Absolute Values of Esophageal Pressure in Subjects With Acute Hypoxemic Respiratory Failure, Mechanically Ventilated in the ICU

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BACKGROUND: A recent trial showed that setting PEEP according to end-expiratory transpulmonary pressure ($P_{pl,ee}$) in acute lung injury/acute respiratory distress syndrome (ALI/ARDS) might improve patient outcome. $P_{pl,ee}$ was obtained by subtracting the absolute value of esophageal pressure (P_{es}) from airway pressure an invariant value of 5 cm H_2O. The goal of the present study was to compare 2 methods for correcting absolute P_{es} values in terms of resulting $P_{pl,ee}$ and recommended PEEP. METHODS: Measurements collected prospectively from 42 subjects with various forms of acute hypoxemic respiratory failure receiving mechanical ventilation in ICU were analyzed. P_{es} was measured at PEEP ($P_{es,ee}$) and at relaxation volume of the respiratory system Vr ($P_{es,Vr}$), obtained by allowing the subject to exhale into the atmosphere (zero PEEP). Two methods for correcting P_{es} were compared: Talmor method ($P_{pl,ee,Talmor} = P_{es,ee} – 5$ cm H_2O), and Vr method ($P_{es,ee,Vr} = P_{es,ee} – P_{es,Vr}$). The rationale was that $P_{es,Vr}$ was a more physiologically based correction factor than an invariant value of 5 cm H_2O applied to all subjects. RESULTS: Over the 42 subjects, median and interquartile range of $P_{es,ee}$ and $P_{es,Vr}$ were 11 (7–14) cm H_2O and 8 (4–11) cm H_2O, respectively. $P_{pl,ee,Talmor}$ was 6 (1–8) cm H_2O, and $P_{es,ee,Vr}$ was 2 (1–5) cm H_2O ($P = .008$). Two groups of subjects were defined, based on the difference between the 2 corrected values. In 28 subjects $P_{pl,ee,Talmor}$ was ≥ $P_{es,ee,Vr}$ (7 [5–9] cm H_2O vs 2 [1–5] cm H_2O, respectively), while in 14 subjects $P_{es,ee,Vr}$ was > $P_{pl,ee,Talmor}$ (2 [0–4] cm H_2O vs −1 [−3 to 2] cm H_2O, respectively). $P_{pl,ee,Vr}$ was significantly greater than $P_{pl,ee,Talmor}$ (7 [5–11] cm H_2O vs 5 [2–7] cm H_2O) in the former, and significantly lower in the latter (1 [−2 to 6] cm H_2O vs 6 [4–9] cm H_2O). CONCLUSIONS: Referring absolute P_{es} values to Vr rather than to an invariant value would be better adapted to a patient's physiological background. Further studies are required to determine whether this correction method might improve patient outcome. *Key words: acute lung injury; ARDS; transpulmonary pressure; esophageal pressure; esophageal manometry.* [Respir Care 2012;57(12):2045–2051. © 2012 Daedalus Enterprises]

Introduction

Loring et al[1] assessed transpulmonary pressure (P_L) using absolute values of esophageal pressure (P_{es}) minored by an invariant value of 5 cm H_2O, in order to take into account the ventral-to-dorsal pleural pressure gradient across the thorax height, the weight of the mediastinum, and the pressure within the balloon.[2] Indeed, in patients with acute lung injury (ALI)/acute respiratory distress syndrome (ARDS) receiving invasive mechanical ventilation in the supine position in the ICU, the absolute values of P_{es} at end-expiration ($P_{es,ee}$) are high.[2] Since P_L is computed as the difference between the pressure at the airway opening (P_{ao}) and P_{es}, some marked negative P_L values are

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obtained. In this context, a trial was carried out[3] comparing PEEP set in order to reach at least 0 cm H_2O end-expiratory P_L ($P_{L,ee}$) to PEEP set according to a PEEP-F_{IO_2} table.[4] This trial found some beneficial physiological effects and a trend toward improved patient survival. This approach for PEEP selection is clever, pragmatic, and feasible for bedside implementation. However, several assumptions need to be validated.[5] In particular, the assumption that the systematic subtraction of an invariant value of 5 cm H_2O bias can be used for all patients. Furthermore, other factors for correcting absolute P_{es} values have previously been used in mechanically ventilated acutely ill patients, such as an invariant value of 2.5 cm H_2O,[6] or the P_{es} value obtained at the relaxation volume of the respiratory system (Vr).[7,8] These latter studies used P_{es} at Vr due to intrinsic PEEP concern, whereas it is a less important factor in ALI/ARDS. However, reports indicated that intrinsic PEEP is frequent in this setting[9] for physiological reasons and also as a result from high breathing rate set at the ventilator to maintain minute-ventilation facing low tidal volume.[10] The goal of the present study was to compare 2 methods for correcting absolute $P_{es,ee}$ values: the subtraction of an invariant 5 cm H_2O value (Talmor method), and the subtraction of P_{es} measured at Vr ($P_{es,Vr}$) (Vr method). Our aim was to compare these 2 methods in terms of resulting $P_{L,ee}$ and recommended PEEP. Our hypothesis was that the Vr method allows for a more physiological correction regarding absolute P_{es} and copes better with the individual mechanical properties of the respiratory system than the Talmor method. If this is true, then the $P_{es,ee}$ to which an invariant value of 5 cm H_2O is subtracted to compute the average pleural pressure ($P_{pl,ee,Talmor}$) and the $P_{es,ee}$ from which $P_{es,Vr}$ was subtracted ($P_{es,ee,Vr}$) should be different across all patients. The null hypothesis of the present study was that there is no difference between $P_{pl,ee,Talmor}$ and $P_{es,ee,Vr}$. We therefore analyzed prospectively collected but not previously reported data from an investigation into patients with various forms of acute hypoxemic respiratory failure (ARF).[11]

QUICK LOOK

Current knowledge

The use of transpulmonary pressure, as determined using airway pressure and esophageal pressure, may have utility in setting PEEP in acute respiratory failure. However, there are a multitude of confounding factors that can affect the accuracy of esophageal pressure measurement.

What this paper contributes to our knowledge

Correcting esophageal pressure measurements obtained at relaxation volume of the respiratory system is more accurate than using the 5 cm H_2O offset to account for the ventral-to-dorsal pressure gradient. This method could improve the individualization of setting PEEP in ARDS.

Methods

The methods have been partially described elsewhere[11] and are summarized below.

Subjects

A prospective multicenter physiological investigation was carried out in consecutive intubated and mechanically ventilated patients with ARF in 6 ICUs in Lyon, France, between November 2001 and September 2002. The study was approved by the local ethics committee, Comité Consultatif Pour la Protection des Personnes se Prêtant à la Recherche Biomédicale Lyon-B. Patients were included if they met all of the following criteria: age over 18 years; tracheal intubation and mechanical ventilation; unilateral or bilateral infiltrates on frontal chest radiograph; $P_{aO_2}/F_{IO_2} < 300$ mm Hg; patient examined within the first 5 days following ICU admission; onset of ARF within the last 3 days; continuous intravenous sedation and/or analgesia; and written, informed consent provided by next of kin. Patients were excluded if any of the following criteria were present: chronic interstitial lung disease; thoracic drainage; hemodynamic instability; pregnancy; impossibility to stop administration of inhaled nitric oxide; or informed consent denied.

Clinical Data Collection

At the time of investigation, the following clinical variables were recorded: age, sex, ideal body weight,[4] and Simplified Acute Physiology Score II. ALI and ARDS were defined according to the European-American consensus conference criteria.[12] Unilateral pneumonia was defined as unilateral radiographic infiltrates associated with $P_{aO_2}/F_{IO_2} < 300$ mm Hg and no echocardiographic argument for elevated left atrial pressure. Cardiogenic pulmonary edema was defined as bilateral radiographic lung infiltrates associated with $P_{aO_2}/F_{IO_2} < 300$ mm Hg and increased left atrial pressure assessed by echocardiography. The ARF subjects were therefore classified under 4 groups: namely, ALI, ARDS, unilateral pneumonia, and cardiogenic pulmonary edema.

Equipment

Air flow was measured using a heated pneumotachograph (Fleisch 2, Fleisch, Lausanne, Switzerland) inserted between the endotracheal tube and the Y-piece of the ventilator. The pressure drop across the 2 ports of the pneumotachograph was measured using a differential piezoresistive transducer (TSD160A, ± 2 cm H_2O, Biopac Systems, Santa Barbara, California). Changes in lung volume were obtained through the numeric integration of the air flow signal. P_{ao} was measured proximal to the endotracheal tube using a piezoresistive pressure transducer (Gabarith 682002, Becton Dickinson, Franklin Lakes, New Jersey). Changes in pleural pressure were estimated based on changes in P_{es}, using a thin-walled latex balloon (80 mm length, 1.9 cm external diameter, 0.1 mm thickness), attached to a 80 cm long catheter with 1.9 mm external diameter and 1.4 mm internal diameter (Marquat Génie Biomédical, Boissy-Saint-Léger, France), positioned in the mid-esophagus and inflated with 1 mL of air.

The validity of the P_{es} measurement was assessed in 2 ways. In subjects with occasional spontaneous breaths the airways were occluded at the end of expiration and subjects were asked to make inspiratory efforts. The correct position of the esophageal balloon was ascertained from the correlation between swings in P_{ao} and P_{es} during this maximal effort.[13] In subjects without spontaneous breathing, the esophageal balloon was inserted into the stomach, as shown by substantial positive changes in pressure on the gentle manual compression of the abdominal left upper quadrant. The esophageal balloon was then withdrawn up to the point at which there was no change in P_{es} tracing during the aforementioned maneuver. The esophageal balloon was connected to a differential pressure transducer (Gabarith 682002, Becton Dickinson, Franklin Lakes, New Jersey). The equipment was calibrated just before each experiment.

The same ventilator (Horus, Taema/Air Liquide Medical Systems, Antony, France) was provided by the Taema company to each participating ICU for the purposes of this study. During measurement, the humidifier was bypassed, and a single-use low-compliance ventilator tube, 60 cm long and with an internal diameter of 2 cm, was used. $\dot{V}$, P_{ao}, and P_{es} signals were recorded on a laptop computer equipped with data-acquisition software (MP 100, Biopac Systems, Goleta, California). The records were stored and subsequently analyzed using software (Acknowledge 3.7.1, Biopac Systems, Goleta, California).

Protocol

Measurements were taken with the subjects in the semi-recumbent position. The subjects were sedated with midazolam (0.2–0.4 mg/kg) and fentanyl (1–3 μg/kg) and paralyzed with atracurium (0.3–0.5 mg/kg) for the purposes of the study. The patient was connected to the study ventilator at the ventilatory settings (volume-controlled mode under constant air flow inflation) established by the physician in charge, which were kept constant for each patient throughout the experiment. While at the PEEP set by the clinician, the subjects first underwent a 3-second end-expiratory occlusion, followed by a 5-second end-inspiratory occlusion. Then, baseline ventilation was resumed, and after 5–15 breaths, PEEP was removed and the patient was manually disconnected from the ventilator to exhale passively to Vr (Fig. 1). Vr was achieved whenever expiratory flow became nil and end-expiratory occlusion did not result in any further increase in P_{ao} (see Fig. 1). The difference between the end-expiratory lung volume during mechanical ventilation in the breath preceding disconnection to Vr was termed the change in functional residual capacity (ΔFRC).

Data Analysis

Three P_{es} measurements were taken. $P_{es,ee}$ was recorded at the end of expiration during baseline ventilation, $P_{es,ee,o}$ at the end of the expiratory occlusion, and $P_{es,Vr}$ at the end of ventilator disconnection. The values of $P_{es,ee}$, $P_{es,ee,o}$, and $P_{es,Vr}$ were averaged over 2 cardiac artifacts in the corresponding frames of the records (see Fig. 1). $P_{pl,ee,Talmor}$ and $P_{pl,ee,o,Talmor}$ were computed as $P_{es,ee}$ or $P_{es,ee,o}$ minus 5 cm H_2O. $P_{es,ee,Vr}$ and $P_{es,ee,oVr}$ were computed as $P_{es,ee}$ or $P_{es,ee,o}$ minus $P_{es,Vr}$. $P_{L,ee}$ was computed as P_{ao} measured at the end of expiration during baseline ventilation ($P_{ao,ee}$) minus $P_{es,ee}$. $P_{L,ee,Talmor}$ was computed as $P_{ao,ee}$ minus $P_{pl,ee,Talmor}$, and $P_{L,ee,Vr}$ as $P_{ao,ee}$ minus $P_{es,ee,Vr}$. Total P_L ($P_{L,ee,o}$) was computed as P_{ao} measured at the end of the expiratory occlusion ($P_{ao,ee,o}$) minus $P_{es,ee,o}$. $P_{L,ee,o,Talmor}$ was equal to $P_{ao,ee,o}$ minus $P_{pl,ee,o,Talmor}$, and $P_{L,ee,oVr}$ to $P_{ao,ee,o}$ minus $P_{es,ee,oVr}$. The plateau pressure of the respiratory system ($P_{plat,rs}$) was measured from the P_{ao} tracing 5 seconds after the onset of the end-inspiratory occlusion.

Finally, the following 2 groups were defined according to the differences in $P_{es,ee}$ and $P_{es,ee,o}$ between the 2 methods for P_{es} correction (corrected groups): corrected group Vr > Talmor, in which $P_{es,ee,Vr}$ or $P_{es,ee,oVr}$ were $\geq P_{pl,ee,Talmor}$ or $P_{pl,ee,o,Talmor}$, and corrected group Talmor > Vr where the opposite was true. That means that $P_{es,Vr}$ was $\leq$ 5 cm H_2O in the first corrected group, and > 5 cm H_2O in the second corrected group.

Statistical Analysis

The normal distribution of the variables across the 42 subjects was verified using the Shapiro-Wilk test. The quantitative values are expressed as median and interquartile range. Values were compared using nonparametric tests or parametric tests, depending on the distribution of the variable. *P* value of < .05 was set as the threshold of statistical significance. The statistical analyses were per-

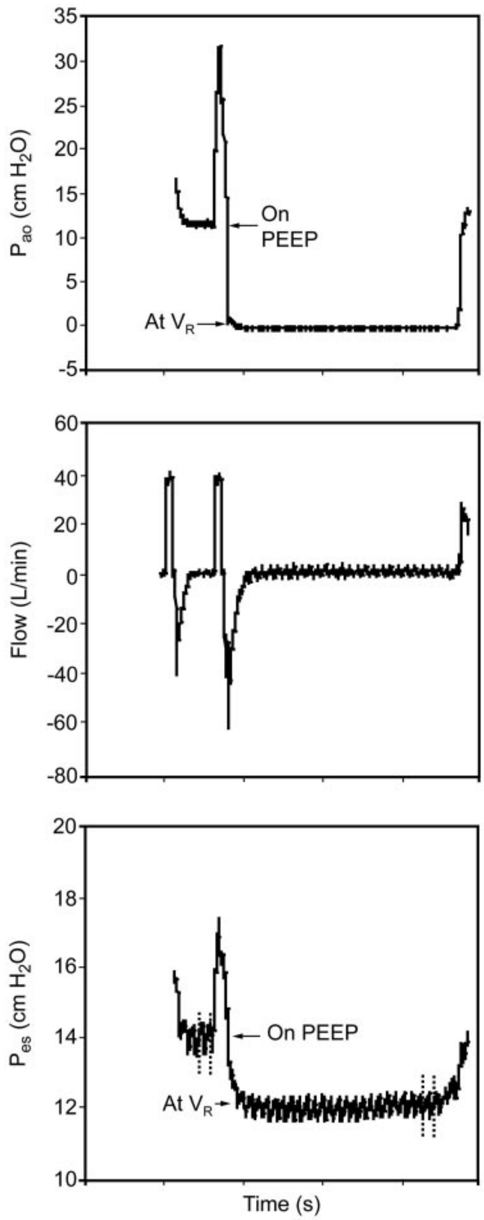

Fig. 1. From top to bottom, records of pressure at the airway opening (P_{ao}), flow, and absolute esophageal pressure (P_{es}) over time in a representative patient. P_{es} was taken at 2 levels of end-expiratory pressure: on PEEP ($P_{ao,ee}$), during baseline ventilation ($P_{es,ee}$), and on zero end-expiratory pressure at the relaxation volume of the respiratory system (Vr) ($P_{es,Vr}$). Each value was averaged between the 2 respective pairs of broken vertical lines.

formed using statistics software (SPSS 17.0, SPSS, Chicago, Illinois).

Results

The present study included 6 subjects not included in the original study due to negative values for the point of maximal compliance increase, obtained by fitting the volume-pressure curve of the respiratory system data points to a sigmoidal equation.[11] Therefore, the present study reported on 42 subjects, whose main characteristics are shown in the Table. The median (IQR) time required to reach Vr was 5 (4–6) seconds beyond the baseline expiratory time, whose median (IQR) value was 2.2 (1.9–2.8) seconds. The uncorrected values of the variables were normally distributed. The same was true for the corrected values, except for $P_{es,ee,Vr}$, $P_{es,ee,oVr}$, $P_{L,ee,Talmor}$ and $P_{L,ee,o,Talmor}$.

Across the 42 subjects, the raw values of $P_{es,ee}$, $P_{es,ee,o}$, and $P_{es,Vr}$ amounted to 11 (7–14) cm H_2O, 11 (7–14) cm H_2O, and 8 (4–11) cm H_2O, respectively (Fig. 2). They were not significantly different between the 4 ARF groups (one-way analysis of variance). The values for $P_{es,ee,Vr}$ and $P_{es,ee,oVr}$ were significantly lower than for their Talmor counterparts, 2 (1–5) cm H_2O versus 6 (1–8) cm H_2O, and 2 (1–5) cm H_2O versus 6 (2–8) cm H_2O, respectively (Fig. 3A, Wilcoxon signed-rank test on matched pairs). As a result, the values of $P_{L,ee,Vr}$ and $P_{L,ee,oVr}$ were significantly higher than those pertaining to Talmor correction (see Fig. 3B, Wilcoxon signed-rank test on matched pairs).

The corrected values for P_{es} were not homogeneous across the 42 subjects. Indeed, in 28 subjects (two thirds of the total) $P_{pl,ee,Talmor}$ was equal (3 tie) to, or greater than $P_{es,ee,Vr}$ (7 [5–9] cm H_2O vs 2 [1–5] cm H_2O, respectively), while in 14 subjects (one third of the total) $P_{es,ee,Vr}$ was greater than $P_{pl,ee,Talmor}$ (2 [0–4] cm H_2O vs −1 (−3

Table. Characteristics of the 42 Subjects at Entry

ARDS, no.	17 (13 primary)
Acute lung injury, no.	13 (9 primary)
Unilateral pneumonia, no.	8
Cardiogenic pulmonary edema, no.	4
Days of investigation	3 (1–4)
Simplified Acute Physiology Score II	58 (43–73)
Age, y	66 (54–74)
Male/female, no.	31/11
Body mass index, kg/m^2	26 (23–28)
Actual weight, kg	79 (68–85)
Height, m	1.70 (1.67–1.76)
Ideal body weight, kg computed from height	66 (57–71)
Tidal volume, mL/kg ideal body weight	7.9 (7.0–8.6)
PEEP, cm H_2O	8 (6–10)
F_{IO_2}	0.50 (0.40–0.70)
P_{aO_2}/F_{IO_2}, mm Hg	191 (145–241)
P_{aCO_2}, mm Hg	42 (36–50)
pH	7.38 (7.33–7.44)

Values are median (IQR) unless otherwise noted.

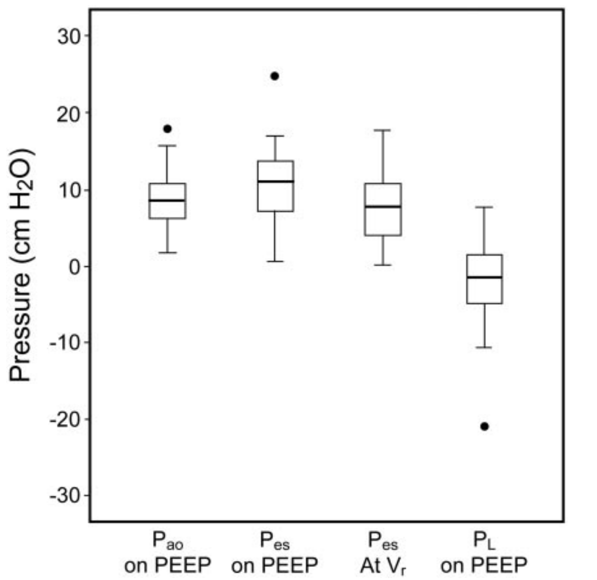

Fig. 2. Box and whisker plot of PEEP applied at the airway opening ($P_{ao,ee}$) and at the chest wall ($P_{es,ee}$), esophageal pressure recorded at the relaxation volume of the respiratory system ($P_{es,Vr}$) on zero end-expiratory pressure and across the lung ($P_{L,ee}$), computed as $P_{ao,ee}$ minus $P_{es,ee}$. Black dots are outliers.

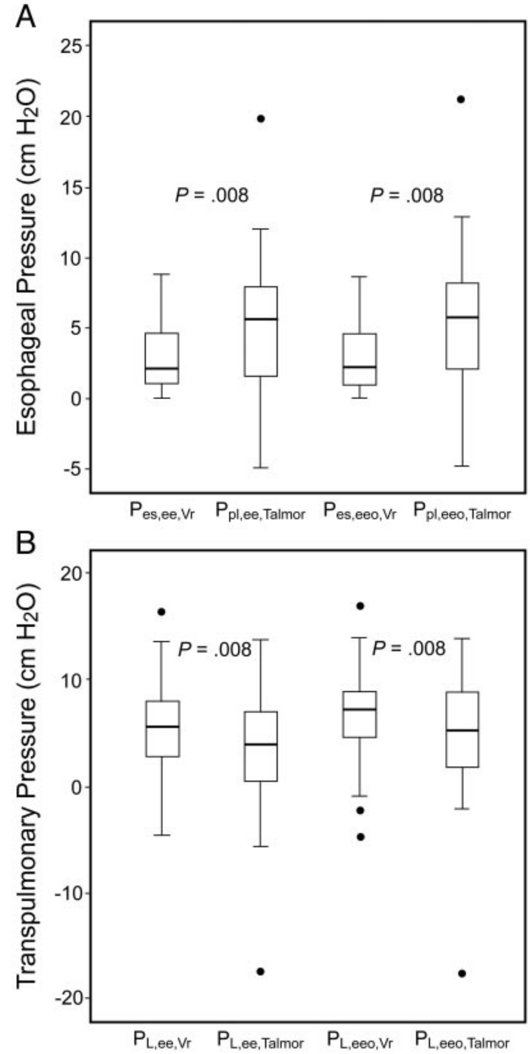

Fig. 3. A. Box and whisker plots of esophageal pressure recorded at end-expiration ($P_{es,ee}$) or at the end of end-expiratory occlusion ($P_{es,ee,o}$), corrected according to the relaxation volume of the respiratory system (Vr) or by subtracting 5 cm H_2O (Talmor method). B. Box and whisker plots of transpulmonary pressure recorded at end-expiration ($P_{L,ee}$) or at the end of end-expiratory occlusion ($P_{L,ee,o}$) corrected according to the relaxation volume of the respiratory system (Vr) or by subtracting 5 cm H_2O (Talmor). * $P = .008$ between groups (Wilcoxon signed-rank test on matched pairs). Black dots are outliers.

to 2) cm H_2O, respectively) (Fig. 4). The same was true for $P_{es,ee,o}$ (not shown). The 2 corrected groups were similar for all variables recorded at entry (see Table), and their rate of occurrence was the same across the ARF groups. Accordingly, the values for $P_{L,ee,Vr}$ were significantly greater than $P_{L,ee,Talmor}$, amounting to 7 (5–11) cm H_2O versus 5 (2–7) cm H_2O ($P < .001$) in the corrected group $P_{pl,ee,Talmor} > P_{es,ee,Vr}$ (Fig. 5), and the values for $P_{L,ee,Talmor}$ were significantly greater than $P_{L,ee,Vr}$ in the other corrected group, amounting to 6 (4–9) cm H_2O versus 1 (−2 to 6) cm H_2O ($P < .001$) (see Fig. 5). The same was true for $P_{L,ee,o}$ (not shown).

The value for ΔFRC (301 (309–494) mL) was not statistically significantly different, either between the 2 corrected groups or across the 4 ARF groups.

The value of $P_{plat,rs}$ was 23 (20–27) cm H_2O in the 42 subjects. There were no significant differences in $P_{plat,rs}$ between the corrected groups across ARF categories (not shown).

Discussion

In the present study we found that the difference in $P_{es,ee}$ between the 2 methods for P_{es} correction was different across the subjects, and the 2 methods for P_{es} correction led to significant differences in terms of $P_{L,ee}$ and, hence, in recommended PEEP.

Vr is the static elastic equilibrium volume of the respiratory system. At that point, the elastic properties of the chest wall are equal in magnitude and act in opposition to those of the lung. This position was taken as the reference for P_{es} values in the present study. For the purposes of the present study, this is an appropriate reference point because it takes into account the physiological characteristics of the respiratory system on an individual basis. It has already been used by other investigators for the same purpose[7,8] in patients with COPD, in whom the end-expiratory lung volume on zero end-expiratory pressure is higher than Vr. This method for dealing with absolute values of

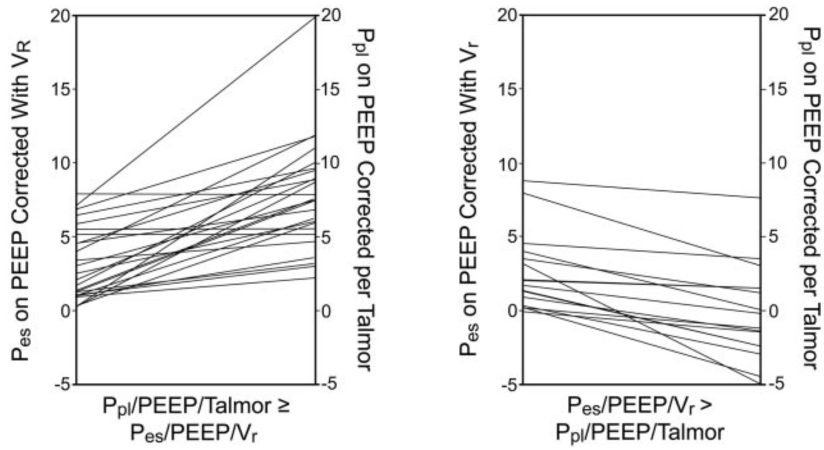

Fig. 4. Individual values of esophageal pressure recorded at end-expiration ($P_{es,ee}$) and corrected either according to relaxation volume of the respiratory system (Vr) or by subtracting 5 cm H_2O from the absolute values (Talmor method) in each group of subjects, depending on the P_{es} correction. *P* was $< .001$ for Vr versus Talmor method in each subset (Wilcoxon signed-rank test on matched pairs).

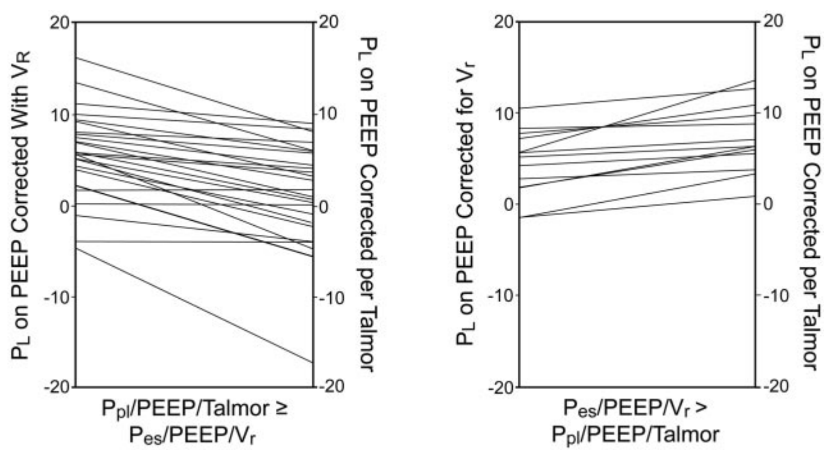

Fig. 5. Individual values of transpulmonary end-expiratory pressure corrected for Vr ($P_{L,ee,Vr}$) or using the Talmor method ($P_{L,ee,Talmor}$) in each group of subjects depending on the P_{es} correction. *P* was $< .001$ for Vr versus Talmor method in each group (Wilcoxon signed-rank test on matched pairs).

P_{es} has not been used in patients with ALI/ARDS. In the present study, unselected patients with various forms of hypoxemic ARF receiving invasive mechanical ventilation in 6 different ICUs were investigated. Therefore, this sample of patients can be seen as representative of the various impaired mechanical conditions under which both correction methods can be tested. The 2 methods for correcting absolute values of P_{es} both produced different results on average. This means that, on average, Vr was statistically significantly different from 5 cm H_2O.

The corrected values for P_{es} differed across subjects, with 2 subsets being identified (see Fig. 4). In 3 subjects only $P_{es,Vr}$ was equal to 5 cm H_2O. This distinction was not dependent on their ARF category. Furthermore, the values for ΔFRC were the same in both subsets of subjects and also across the ARF categories. Therefore, the results for the 2 correction methods cannot be explained by differences in end-expiratory lung volume or the nature of the ARF. The difference between the 2 methods of correction is specific to each patient's individual circumstances. Since Vr is more physiologically relevant than an invariant value of 5 cm H_2O, the present results suggest referring absolute P_{es} to its value at Vr. This method is patient-centered and would correct absolute P_{es} values according to the physiological context. However, this strategy requires a specific maneuver that may induce lung derecruitment, since PEEP has to be removed and time allowed before zero flow is reached (see Fig. 1). The median time required to reach Vr was 5 seconds in the present study, which may not be a major issue. To mitigate this potential problem, one would perform a recruitment maneuver after prolongation of expiration. It can be argued that the reproducibility of Vr was not ascertained, since an invariant value was used. The same, however, is true when subtracting the single value of 5 cm H_2O.

The values for $P_{L,ee,Vr}$ were significantly greater than $P_{L,ee,Talmor}$. Therefore, using the Vr correction method would result in setting higher PEEP values. The question of high versus low PEEP in ALI/ARDS is not fully resolved. Indeed, the meta-analysis of individual data showed no difference in mortality between higher and lower PEEP in ALI/ARDS.[14] However, the subgroup of ARDS patients had a significantly lower mortality when receiving higher rather than lower PEEP.[14] The results obtained by Talmor et al[3] support this finding. In the present study, Vr correction would have generated a PEEP level greater than 1.7 cm H_2O (median) above the actual level set by the clinician, with no significant change in $P_{plat,rs}$, regardless of ARF category. It should be stressed that the present study did not address the issue of patient outcome. Therefore, further studies should be done to explore whether the Vr correction method for P_{es} would impact on patient outcome.

Conclusions

In conclusion, referring absolute P_{es} values to Vr would better improve the customization of the correction of P_{es} based on the physiological and individual context, rather than an invariant value of 5 cm H_2O.

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